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10/538,534	06/10/2005	Wayne D. Frasch	112624.00089	4137
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RENAISSANC	E ONE		SHAW, AMANDA MARIE	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

1.						
		Application No.	Applicant(s)			
Office Action Summary		10/538,534	FRASCH ET.AL.			
		Examiner	Art Unit			
		Amanda M. Shaw	1634			
The MAILING DATE of this communication appears on the cover sheet with the correspondence address Period for Reply						
A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION. - Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication. - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication. - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).						
Status						
1)⊠	Responsive to communication(s) filed on <u>15 May 2007</u> .					
'=	This action is FINAL . 2b) ☐ This action is non-final.					
3)	Since this application is in condition for allowance except for formal matters, prosecution as to the merits is					
closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11, 453 O.G. 213.						
Disposition of Claims						
 4) Claim(s) 1-3,5-11,13-17,26-28 and 30-39 is/are pending in the application. 4a) Of the above claim(s) is/are withdrawn from consideration. 5) Claim(s) is/are allowed. 6) Claim(s) 1-3, 5-11, 13-17, 26-28, and 30-39 is/are rejected. 7) Claim(s) is/are objected to. 8) Claim(s) are subject to restriction and/or election requirement. 						
Application Papers						
10)⊠	The specification is objected to by the Examiner The drawing(s) filed on 10 June 2005 is/are: a) Applicant may not request that any objection to the Replacement drawing sheet(s) including the correction The oath or declaration is objected to by the Example 1.	☑ accepted or b)☐ objected to drawing(s) be held in abeyance. See on is required if the drawing(s) is object.	e 37 CFR 1.85(a). jected to. See 37 CFR 1.121(d).			
Priority (under 35 U.S.C. § 119					
 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f). a) All b) Some * c) None of: 1. Certified copies of the priority documents have been received. 2. Certified copies of the priority documents have been received in Application No. 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)). * See the attached detailed Office action for a list of the certified copies not received. 						
2) Notice 3) Information	et(s) ce of References Cited (PTO-892) ce of Draftsperson's Patent Drawing Review (PTO-948) mation Disclosure Statement(s) (PTO/SB/08) er No(s)/Mail Date	4) Interview Summary Paper No(s)/Mail Da 5) Notice of Informal P 6) Other:	ate			

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DETAILED ACTION

1. This action is in response to the amendment filed May 15, 2007. This action is made FINAL.

Claims 1-3, 5-11, 13-17, 26-28, 30-32, and 38-39 are currently pending. Claims 1, 8, 9, 17, and 26 have been amended. Claims 38 and 39 are newly presented.

Therefore Claims 1-3, 5-11, 13-17, 26-28, 30-32, and 38-39 will be addressed herein.

Withdrawn Objections

2. The objections made over Claims 8 and 17 in the second paragraph of the Office Action of January 18, 2007 are withdrawn in view of the amendments made to the claims.

Withdrawn Rejections

3. The rejections made over Claims 1-7, 9-16, and 26-32 under 35 USC 103(a) in the third paragraph of the Office Action of January 18, 2007 are withdrawn in view of amendments made to the claims.

The rejections made over Claims 8 and 17 under 35 USC 103(a) in the fourth paragraph of the Office Action of January 18, 2007 are withdrawn in view of amendments made to the claims.

Claim Objections

4. THE FOLLOWING IS A NEW GROUND OF OBJECTION NECESSITATED BY APPLICANTS AMENDMENTS TO THE CLAIMS:

Claims 5, 6, 13, 14, 30, and 31 are objected to because of the following informalities: each of these claims depend from claims that have been cancelled. For example Claim 5 depends on "the method of claim 4", however claim 4 has been cancelled. Appropriate correction is required.

Claim Rejections - 35 USC § 103

- 5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:
 - (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. THE FOLLOWING IS A NEW GROUND OF REJECTION NECESSITATED BY APPLICANTS AMENDMENTS TO THE CLAIMS:

Claims 1-3, 5-7, 9-11, 13-16, 26-28, 30-32, and 38-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yasuda et al (Nature 2001) in view of Yu (The Journal of Physical Chemistry 1997) and in further view of Pettingell et al (US Patent 6449088 Filed 1993) as evidenced by Kudo (Nature 1990).

Regarding Claims 1-3 and 5-7 Yasuda et al teaches a molecular structure having a rotating arm (F1-ATPase enzyme) (Abstract). Yasuda et al further teaches attaching a nanoparticle (40 nm bead) to the rotating arm of the molecular structure so that the nanoparticle rotates with the rotating arm of the molecular structure (See Fig 1). Yasuda further teaches that bead rotation was imaged by laser dark field microscopy (Page 898).

Yasuda et al does not teach attaching a nanoparticle having a first and second axis to the rotating arm wherein the first axis is longer than the second axis. Further Yasuda et al does not teach a method wherein the first axis of the nanoparticle scatters a first wavelength of light when the nanoparticle is in a first position of rotational motion and the second axis of the nanoparticle scatters a second wavelength of light when the nanoparticle is in a second position of rotational motion. Yasuda does not teach a method wherein the nanoparticle is rod shaped. Yasuda does not teach a method wherein the nanoparticle is a gold nanorod. Yasuda does not teach a method wherein the first wavelength of light is longer than the second wavelength of light and the first wavelength of the light is red and the second wavelength of the light is green.

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However Yu et al teaches gold nanorods that have a first axis and second axis wherein the first axis is longer than the second axis (See Figure 1). Yu et al further teach that gold nanorods have two different surfaces and thus have two surface plasmon resonances due to the anisotropy of the shape. The dominant SP1 band corresponds to longitudinal resonance and when exposed to light scatters a longer wavelength (red). The weaker band corresponds to transverse resonance and when exposed to light scatters a shorter wavelength (green) (Page 6662 and 6664). Thus if these nanorods where attached to a rotating arm, the first axis of the nanoparticle would scatter a first wavelength of light when the nanoparticle is in a first position of rotational motion and the second axis of the nanoparticle scatters a second wavelength of light when the nanoparticle is in a second position of rotational motion.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Yasuda et al by using a gold nanorod in place of a nanosphere and detecting rotation by observing alternating first and second rotations of light as suggested by Yu. A method which uses a gold nanorod opposed to a gold nanosphere makes it possible to observe a rotational motion because gold nanospheres have two different surface plasmon resonances which makes it possible to observe alternating first and second wavelengths of light, while gold nanospheres only have one surface plasmon resonance and only produce a single wavelength of light as taught by Yu (Page 6662 and 6664).

Additionally it is noted that Yasuda teaches using a dark field microscope to observe rotation but does not describe how the microscope works. Therefore Yasuda

does not teach a method comprising providing light from a fixed location, altering a path of the light to create an oblique angle with respect to the first and second axis of the nanoparticle, exposing the light from the altered path onto the nanoparticle, providing an iris which passes the first and second wavelengths of scatted light and blocks unscattered light, providing a polarizing filter which is aligned only to the first and second wavelength of light wherein the polarizing filter blocks light not aligned with the filter, processing the first and second wavelength of light from the polarizing filter through optical processing equipment to separate the first and second wavelengths into first and second channels, detecting alternating first and second wavelengths by absence of light between each alternating first and second wavelength which indicates motion of the nanoparticle and molecular structure and detecting no light which indicates absence of motion of the nanoparticle and molecular structure.

However Pettingell et al teach a dark field microscope comprising a light source (Column 1, line 33). The path of the light is altered using a reflector which creates light at oblique angles with respect to the object being detected (Column 1, line 33). The light from the altered path hits the object which scatters the light which enters the iris (i.e. pupil). Unscattered light (i.e. light that does not hit the object) does not enter the iris (i.e. pupil) (Column 2, lines 1-15). Pettingell also discloses using polarizing filters. Specifically Pettingell teaches that polarizing filters can be used to look at anisotropic materials (e.g., materials that have a first and second axis) (Column 3, lines 10-15). The polarizing filters are used to separate the first and second wavelengths of light generated by anisotropic materials. While Pettingell does not specifically say that the

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motion can be detected by detecting alternating first and second wavelengths by absence of light between each alternating first and second wavelength and that the absence of motion can be detected by detecting no light, it is property of the method that this could be done. This is evidenced by Kudo (Nature) who teaches using dark field microscopy to detect rotation. Specifically Kudo teaches that alternating increases and decreases of light intensity are observed and each cycle corresponds to one rotation (Page 679) Kudo also teaches that the speed of rotation can be determined by the rate of alternating first and second wavelengths of light (Figure 4).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Yasuda et al by using the dark field microscope of Pettingell to detect rotation of the molecular motor. Methods of using dark field microscopy were well known in the art at the time of the invention as demonstrated by Pettingell and were particularly useful for detecting rotational movements as evidenced by Kudo. Thus it would have been obvious to an ordinary artisan to use dark field microscopy in situations wherein one wanted to analyze molecular rotations in more detail.

Regarding Claims 9-11 and 13-16 Yasuda et al teaches a molecular structure having a rotating arm (F1-ATPase enzyme) (Abstract). Yasuda et al further teaches attaching a nanoparticle (40 nm bead) to the rotating arm of the molecular structure so that the nanoparticle rotates with the rotating arm of the molecular structure (See Fig 1).

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Yasuda further teaches that bead rotation was imaged by laser dark field microscopy (Page 898).

Yasuda et al does not teach attaching a nanoparticle to a rotating portion of a molecular structure wherein a first axis of the nanoparticle has a greater length than a second axis. Further Yasuda et al does not teach a method wherein the first axis of the nanoparticle scatters a first wavelength of light when the nanoparticle is in a first position of rotational motion and the second axis of the nanoparticle scatters a second wavelength of light when the nanoparticle is in a second position of rotational motion. Yasuda does not teach a method wherein the nanoparticle is rod shaped. Yasuda does not teach a method wherein the nanoparticle is a gold nanorod. Yasuda does not teach a method wherein the first wavelength of light is longer than the second wavelength of light and the first wavelength of the light is red and the second wavelength of the light is green.

However Yu et al teaches gold nanorods that have a first axis and second axis wherein the first axis is longer than the second axis (See Figure 1). Yu et al further teach that gold nanorods have two different surfaces and thus have two surface plasmon resonances due to the anisotropy of the shape. The dominant SP1 band corresponds to longitudinal resonance and when exposed to light scatters a longer wavelength (red). The weaker band corresponds to transverse resonance and when exposed to light scatters a shorter wavelength (green) (Page 6662 and 6664). Thus if these nanorods where attached to a rotating arm, the first axis of the nanoparticle would scatter a first wavelength of light when the nanoparticle is in a first position of rotational

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motion and the second axis of the nanoparticle scatters a second wavelength of light when the nanoparticle is in a second position of rotational motion.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Yasuda et al by using a gold nanorod in place of a nanosphere and detecting rotation by observing alternating first and second rotations of light as suggested by Yu. A method which uses a gold nanorod opposed to a gold nanosphere makes it possible to observe a rotational motion because gold nanospheres have two different surface plasmon resonances which makes it possible to observe alternating first and second wavelengths of light, while gold nanospheres only have one surface plasmon resonance and only produce a single wavelength of light as taught by Yu (Page 6662 and 6664).

Additionally it is noted that Yasuda teaches using a dark field microscope to observe rotation but does not describe how the microscope works. Therefore Yasuda does not teach a method comprising exposing a light to the first axis of the nanoparticle to scatter a first wavelength of the light when the nanoparticle is in a first position, exposing a light to the second axis to scatter a second wavelength of light when the nanoparticle is in a second position, filtering the scattered light to pass only the first and second wavelengths of the light a block unscattered light, detecting alternating first and second wavelengths by absence of light between each alternating first and second wavelength which indicates motion of the nanoparticle and molecular structure, and detecting no light which indicates absence of motion of the nanoparticle and molecular structure.

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Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Yasuda et al by using the dark field microscope of Pettingell to detect rotation of the molecular motor. Methods of using dark field microscopy were well known in the art at the time of the invention as

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demonstrated by Pettingell and were particularly useful for detecting rotational movements as evidenced by Kudo. Thus it would have been obvious to an ordinary artisan to use dark field microscopy in situations wherein one wanted to analyze molecular rotations in more detail.

Regarding Claims 26-28 and 30-32 Yasuda et al teaches a molecular structure having a rotating arm (F1-ATPase enzyme) (Abstract). Yasuda et al further teaches attaching a nanoparticle (40 nm bead) to the rotating arm of the molecular structure so that the nanoparticle rotates with the rotating arm of the molecular structure (See Fig 1). Yasuda further teaches that bead rotation was imaged by laser dark field microscopy (Page 898).

Yasuda et al does not teach attaching an anisotropic particle to a rotating portion of a molecular structure wherein a first axis of the anisotropic particle has a greater length than a second axis. Further Yasuda et al does not teach a method wherein the first axis of the anisotropic particle scatters a first wavelength of light when the particle is in a first position of rotational motion and the second axis of the particle scatters a second wavelength of light when the particle is in a second position of rotational motion. Yasuda does not teach a method wherein the anisotropic particle is rod shaped. Yasuda does not teach a method wherein the anisotropic particle is a gold nanorod.

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second wavelength of light and the first wavelength of the light is red and the second wavelength of the light is green.

However Yu et al teaches gold nanorods that have a first axis and second axis wherein the first axis is longer than the second axis (See Figure 1). Yu et al further teach that gold nanorods have two different surfaces and thus have two surface plasmon resonances due to the anisotropy of the shape. The dominant SP1 band corresponds to longitudinal resonance and when exposed to light scatters a longer wavelength (red). The weaker band corresponds to transverse resonance and when exposed to light scatters a shorter wavelength (green) (Page 6662 and 6664). Thus if these nanorods where attached to a rotating arm, the first axis of the nanoparticle would scatter a first wavelength of light when the nanoparticle is in a first position of rotational motion and the second axis of the nanoparticle scatters a second wavelength of light when the nanoparticle is in a second position of rotational motion.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Yasuda et al by using a anisotropic gold nanorod in place of a nanosphere and detecting rotation by observing alternating first and second rotations of light as suggested by Yu. A method which uses a gold nanorod opposed to a gold nanosphere makes it possible to observe a rotational motion because gold nanospheres have two different surface plasmon resonances which makes it possible to observe alternating first and second wavelengths of light, while gold nanospheres only have one surface plasmon resonance and only produce a single wavelength of light as taught by Yu (Page 6662 and 6664).

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However Pettingell et al teach a dark field microscope comprising a light source (Column 1, line 33). The path of the light is altered using a reflector which creates light at oblique angles with respect to the object being detected (Column 1, line 33). The light from the altered path hits the object which scatters the light which enters the iris (i.e. pupil). Unscattered light (i.e. light that does not hit the object) does not enter the iris (i.e. pupil) (Column 2, lines 1-15). Pettingell also discloses using polarizing filters. Specifically Pettingell teaches that polarizing filters can be used to look at anisotropic materials (e.g., materials that have a first and second axis) (Column 3, lines 10-15). The polarizing filters are used to separate the first and second wavelengths of light generated by anisotropic materials. While Pettingell does not specifically say that the motion can be detected by detecting alternating first and second wavelengths by absence of light between each alternating first and second wavelength and that the absence of motion can be detected by detecting no light, it is property of the method

that this could be done. This is evidenced by Kudo (Nature) who teaches using dark field microscopy to detect rotation. Specifically Kudo teaches that alternating increases and decreases of light intensity are observed and each cycle corresponds to one rotation (Page 679) Kudo also teaches that the speed of rotation can be determined by the rate of alternating first and second wavelengths of light (Figure 4).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Yasuda et al by using the dark field microscope of Pettingell to detect rotation of the molecular motor. Methods of using dark field microscopy were well known in the art at the time of the invention as demonstrated by Pettingell and were particularly useful for detecting rotational movements as evidenced by Kudo. Thus it would have been obvious to an ordinary artisan to use dark field microscopy in situations wherein one wanted to analyze molecular rotations in more detail.

7. THE FOLLOWING IS A NEW GROUND OF REJECTION NECESSITATED BY APPLICANTS AMENDMENTS TO THE CLAIMS:

Claims 8 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yasuda et al (Nature 2001) in view of Yu (The Journal of Physical Chemistry 1997) and in further view of Pettingell (US Patent 6449088 Filed 1993) as evidenced by Kudo

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(Nature 1990) as applied to claims 1 and 9 above, and in further view of Felder (US Patent 6232066).

The teachings of Yasuda, Yu, and Pettingell are presented above.

The combined references do not teach a method which further includes a step of disposing a detection DNA strand between the nanoparticle and the molecular structure, wherein the detection DNA strand hybridizes with a target DNA strand, if the target DNA strand matches the detection DNA strand, to form a structural link between the molecular structure and the nanoparticle.

However Felder teach an array of probes comprising anchor oligonucleotides immobilized to the substrate and a linker oligonucleotide attached to the anchor oligonucleotides. In the presence of a target nucleic acid, the target binds to the said linker followed by the hybridization of a detector oligonucleotide which has a reporter (Column 1 line 66 to Column 2 line 3 and Figure 1). Thus the linker oligonucleotide and the target nucleotide form a structural link between the anchor and the nanoparticle.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Yasuda et al by using a nucleic acid strand to attach the nanoparticle to the molecular structure as suggested by Felder because hybridization methods which use linker oligonucleotides attached to a solid support which bind to target nucleotides attached to detection molecules were routinely performed in the art as demonstrated by Felder. One would be motivated to use nucleic acids rather than streptavidin for the benefit of being able to detect hybridization.

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Response To Arguments

In the response filed May 15, 2007, Applicants traversed the 103 rejections made 8. over Yasuda, Yu, and Stevens by stating that the references singularly or in combination do not teach or suggest the steps that have been added to the claims in the Amendment filed May 15, 2007. This argument has been fully considered and was found persuasive; however new rejections have been issued that are believed to teach all of the steps required by claims filed May 15, 2007. The applicants also argued that there is no reason or logic for the examiner to combined the references. The Applicants assert that Yasuda teaches a rotating F1-ATPase enzyme but never considered detecting its motion. This is not true because Yasuda teaches that bead rotation was imaged by laser dark field microscopy (Page 898). By detecting the rotation of the bead, Yasuda also would have been able to detect rotation of the F1-ATPase since the bead is attached to the F1-ATPase. The Applicants further assert that Yu teaches that the long and short axis of gold nanorods scatter different wavelengths of incident light but never considered the present invention combination. While this may be true the Yu reference is only being relied upon for teaching gold nanorods. A method which uses a gold nanorod opposed to a gold nanosphere makes it possible to observe a rotational motion because gold nanospheres have two different surface plasmon resonances which makes it possible to observe alternating first and second wavelengths of light, while gold nanospheres only have one surface plasmon resonance and only produce a single wavelength of light as taught by Yu (Page 6662 and 6664). Thus one would have

been motivated to substitute the gold nanosphere of Yasuda for the gold nanorod of Yu in order to analyze molecular rotation in more detail.

Conclusion

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amanda M. Shaw whose telephone number is (571) 272-8668. The examiner can normally be reached on Mon-Fri 7:30 TO 4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for

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the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Amanda M. Shaw Examiner Art Unit 1634

BJ FORMAN, PH.D. PRIMARY EXAMINER